

## Decision analysis model for paratuberculosis control in commercial dairy herds

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### Abstract

A previous economic test-and-cull decision analysis model has been strengthened and updated with current epidemiologic information. Created using Excel<sup>®</sup> and PrecisionTree<sup>®</sup> software, the model incorporates costs and benefits of herd management changes, diagnostic testing, and different management actions based on test results to control paratuberculosis in commercial dairy herds. This novel “JD-Tree” model includes a herd management decision node (four options), a test/no test decision node (two options), a diagnostic test choice decision node (five options), test result chance nodes (four levels of possible results), and test action decision nodes (three options; cull, manage, no action). The model culminates in a chance node for true infection status. Outcomes are measured as a net cost–benefit value to the producer. The model demonstrates that improving herd management practices to control infection spread (hygiene) is often more cost-effective than testing; not all herds should test as part of a paratuberculosis control program. For many herds, low-cost tests are more useful than more sensitive, higher cost tests. The model also indicates that test-positive cows in early stages of infection may be retained in the herd to generate farm income, provided they are managed properly to limit infection transmission. JD-Tree is a useful instructional tool, helping veterinarians understand the complex interactions affecting the economics of paratuberculosis control and to define the accuracy and cost specifications of better diagnostic tests.

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## 1. Introduction

Paratuberculosis (Johne's disease) is a chronic, progressive, inflammatory gastrointestinal disease of ruminants caused by infection with *Mycobacterium avium* subspecies *paratuberculosis* (*Mycobacterium paratuberculosis*) (Harris and Barletta, 2001). Clinical disease is characterized by diarrhea, weight loss, debilitation, and eventual death. With no legal or cost-effective treatment available, Johne's disease causes substantial economic losses to dairy cattle operations worldwide, primarily as a result of reduced milk yield, reduced slaughter values, increased premature and involuntary culling, decreased fertility, increased mortality rate and increased susceptibility to other diseases (Bakker et al., 2000; Whittington and Sergeant, 2001). The net economic impact of paratuberculosis on the U.S. dairy industry has been estimated at from US\$ 200 to 1500 million annually (Ott et al., 1999; Harris and Barletta, 2001).

According to several studies, *M. paratuberculosis* infects 5–10% of dairy cattle and approximately 33% of dairy herds in the U.S. (Collins et al., 1994; Thorne and Hardin, 1997; Wells and Wagner, 2000; Johnson et al., 2001; Adaska and Anderson, 2003). Based on clinical reports, diagnostic records, historical records, and animal movements due to the ongoing restructuring of the U.S. dairy industry (herd expansions), the incidence of this infection appears to be steadily rising.

Recently, Johne's disease has come under scrutiny from the medical community and the public due to evidence suggesting *M. paratuberculosis* may be responsible for some cases of Crohn's disease in humans (Chamberlin et al., 2001; El Zaatari et al., 2001; Harris and Lammerding, 2001; Hermon-Taylor and Bull, 2002; Naser et al., 2002, 2004; Bull et al., 2003; Greenstein, 2003; Olsen et al., 2003; Ghadiali et al., 2004; Sechi et al., 2004). A definitive link has yet to be established, but if confirmed, a growing number of studies suggest that the retail pasteurized milk supply may be a vehicle for human exposure to *M. paratuberculosis* (Hammer et al., 2002; Grant et al., 2002a,b,c; Ayele et al., 2005; Ellingson et al., 2005).

Control of paratuberculosis requires first and foremost effective herd biosecurity management protocols and possibly the use of diagnostic tests (Harris and Barletta, 2001). Control strategies that require herd-wide testing are a significant financial burden to dairy producers: culling (slaughter of test-positive animals) and herd management changes to limit infection transmission add even more costs. In fact, the efficacy of test-and-cull strategies to control paratuberculosis has been questioned. Data from case histories, and simulation models have led experts to conclude that changing herd management is more effective than test-and-cull programs for paratuberculosis control (Collins and Morgan, 1991a, 1992; Groenendaal et al., 2002; Groenendaal and Galligan, 2003). However, modeling efforts to date have focused solely on the cost–benefit of testing without rigorously scrutinizing the cost–benefit of herd management changes.

Optimizing the overall economic benefit from a paratuberculosis control program depends on many factors including, but not limited to: within-herd prevalence, cost of the disease, cost of the diagnostic test, accuracy of the diagnostic test, actions taken by the producer based on test results, level of sanitation (calf rearing hygiene in particular) on the farm, the costs of attaining a more stringent level of herd hygiene, and the economic state of the dairy industry (i.e. milk price, cull cow price, cost of herd replacements, etc.).

Integration of these factors to define the economically optimal paratuberculosis control program for producers is complex, especially given the diversity in production, animal health and management styles among herds. Decision analysis models clarify the decision making process by comparing alternative courses of action in a structured and efficient manner while providing a means of measuring the net economic outcome of each decision. The objective of this study was to create a decision analysis computer model to weigh varied diagnostic tests and herd management strategies for paratuberculosis control to define the most effective and economically attractive program for commercial dairy producers, i.e., those with the primary business objective of selling milk. The model capitalizes on data from a recent field study that evaluated eight diagnostic tests for paratuberculosis to enhance the validity of the model (Collins et al., 2005).

## 2. Materials and methods

### 2.1. Overview of the decision tree model

A spreadsheet model was developed in Microsoft EXCEL<sup>®</sup> using Precision Tree<sup>®</sup> (Palisade Corporation, Newfield, NY), a decision analysis add-in software program. The model is cross-sectional, that is, decisions are made at one moment in time (on a yearly basis). The key dairy producer decisions modeled concern: (1) the extent of herd management changes made to limit transmission of *M. paratuberculosis*, (2) whether to use diagnostic tests, and, if testing is pursued, which test to use, and (3) what actions to take based on diagnostic test results.

The foundation of the model is a paratuberculosis test-and-cull decision analysis model described by Collins and Morgan (1991a). This new decision tree was constructed with multi-level diagnostic test interpretations using post-test probabilities derived from likelihood ratios and within-herd *M. paratuberculosis* infection prevalence (Sackett et al., 1991). It incorporates elements of a paratuberculosis eradication model using modified Reed–Frost equations to calculate the effect of improved hygiene on the incidence of new *M. paratuberculosis* infections (Collins and Morgan, 1991b, 1992). When model design choices between elaboration and simplification were faced, simplification was preferred, particularly where uncertainty exists about the biology of paratuberculosis (Black and Singer, 1987).

The decision tree model, hereafter called “JD-Tree”, is structured with the following sequential four decision and two chance nodes with their associated branches: “Herd Hygiene Decision”, a decision node with four herd hygiene levels; “Test Decision”, a decision node to test or not test for paratuberculosis; “Test Type Decision”, a decision node with a choice among five different types of diagnostic tests; “Test Result”, a chance node with four levels of test interpretation (high, moderate, low, and negative); “Producer Decision”, a decision node for cow management actions at the four diagnostic test levels; and “True Infection State”, a chance node designating the probability that cows in the testing category are truly *M. paratuberculosis*-infected (Fig. 1). These are ordered to reflect the sequence of decisions made by dairy producers (or more accurately the order in which experts believe these decisions should be made) (Kennedy and Benedictus, 2001).

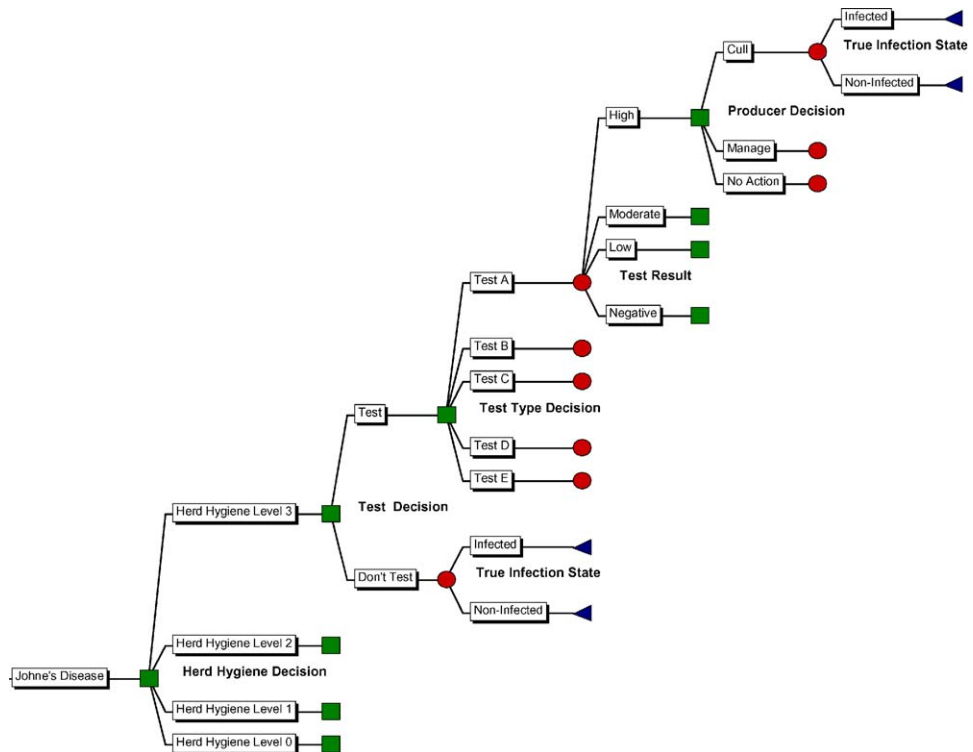


Fig. 1. Simplified diagram of the JD-Tree model.

JD-Tree evaluates “not testing” in comparison to “testing” for paratuberculosis by one of five diagnostic assays designated A, B, C, D, or E. The characteristics of these five tests were generated from field evaluation data for a serum ELISA, milk ELISA, conventional fecal culture, a TaqMan<sup>®</sup> PCR for *M. paratuberculosis* on feces, and fecal culture using liquid media, respectively (Collins et al., 2005). Diagnostic results for all tests were expressed at four levels: high, moderate, low, and negative reflecting the level of antibody or *M. paratuberculosis* bacteria detected in the clinical sample.

Producer decisions based on test results for each cow included culling, managing the cow in a manner to limit spread of *M. paratuberculosis*, or taking no action. JD-Tree serially combines the decision and chance nodes to result in 960 different permutations (four hygiene levels × two test decisions × five test types × four levels of test result × three producer decisions on results × two outcomes) that, together with economic outcomes for each end event, are used by the program to define the economically optimal path through the tree. The structure of the tree includes paths commonly not considered economically sound (e.g. culling a test-negative cow without clinical signs of paratuberculosis). These paths served as internal controls allowing verification of the model results.

JD-Tree results are expressed as cost (US\$) per adult cow (2 years of age) per year, including all management changes, testing costs and cow culling or management decisions. Herd characteristics including milk production were input variables. As a

reference point, these were initially set to represent a typical mid-sized commercial dairy herd in the U.S., hereafter referred to as the “Base Herd”: 100 dairy cows and a 10% within-herd true prevalence of *M. paratuberculosis*-infection (Table 1). The base milk price was set at US\$ 0.276/kg (US\$ 12.50/100 lb) and base rolling herd average (RHA) was 9759 kg (21,470 lb) (Wisconsin Agricultural Statistics Service, <http://www.nas.usda.gov/wi/>). Herd size in the model does not change, so the number of culls per year equals the number of replacements per year. Base herd cull rate was set at 0.37 and birth rate at 0.86.

All economic values in the model were set to zero for a herd at the lowest hygiene level (HH-0) that did not test for the infection, thus establishing a baseline for determining the net cost–benefit of control strategies in the model. This net value was the economic effect of a selected paratuberculosis control strategy in a herd of the same size and paratuberculosis prevalence, relative to a herd at the lowest hygiene level and not testing.

## 2.2. Cost of paratuberculosis

The economic impact of paratuberculosis may be classified into direct, indirect, and unapparent costs (Kennedy and Benedictus, 2001). Direct costs included in the model are those associated with reduced milk production, increased mortality rate, infertility, and lost slaughter value due to decreased cull cow weight (not realized until the time of culling).

Milk production losses associated with paratuberculosis vary considerably among published studies (Benedictus et al., 1987; McNab et al., 1991; Wilson et al., 1993; Johnson et al., 2001). For this model, the cost of paratuberculosis due to decreased milk production by *M. paratuberculosis*-infected cows was calculated based on a 4% decrease in RHA milk production (Nordlund et al., 1996).

Impaired fertility due to paratuberculosis has been demonstrated: *M. paratuberculosis* ELISA-positive cows had a 28-day increase in days open when compared to ELISA-negative cows (Johnson-Ifeorulundu et al., 2000). For the model, each additional day added to the calving interval cost the producer US\$ 2.00 and therefore included a net loss of US\$ 56 for decreased reproductive performance of each *M. paratuberculosis*-infected cow (Pecsok et al., 1994).

Table 1  
Characteristics of the base herd and baseline economic values used in the JD-Tree model

Parameter	Value
Herd size ( <i>H</i> )	100
Replacement rate (cull rate)	0.37
Birth rate ( <i>Br</i> )	0.86
Calving interval (months)	14
Rolling herd average (RHA); kg/cow/yr (lb/cow/yr)	9759 (21470)
True infection prevalence (% adult herd)	0.10
Milk price; US\$/kg (US\$/100 lb)	US\$ 0.276 (US\$ 12.50)
Slaughter value (SV); US\$/kg live weight (US\$/lb)	US\$ 1.03 (US\$ 0.47)
Replacement heifer cost (RHC)	US\$ 1500.00
Test-positive cow management ability	2
Replacement source classification	3

The mortality rate for infected herds was 3% higher than for noninfected herds in the model (Johnson-Ifeorulundu et al., 1999). The increase in mortality rate results in economic losses due to both replacement heifer cost (RHC) and loss of salvage value (SV) from slaughter.

Although owners of heavily *M. paratuberculosis*-infected herds recognize increased cull rates as one of the major economic burdens associated with the disease, it is difficult to estimate the cost. Increased cull rate is one of the unapparent costs associated with premature involuntary culling (IC) and as such was included in the model as a component of the disease cost equation. Lost opportunity cost due to premature involuntary culling results in lost future income that decreases profit by: increasing replacement costs (more replacements must be raised); increasing herd health costs (more cows with health problems) due to the inability of the producer to selectively cull for other diseases; decreasing the average age of cows in the herd, which decreases the proportion of cows that are at higher milk production; and, decreasing opportunities for culling low producing cows, which also decreases average production per cow in the herd. Some have estimated that the decreased lifetime production of cows due to premature culling and slowed genetic improvement of a herd due to involuntary culling of genetically valuable animals is US\$ 500 per clinical case of paratuberculosis due to unrealized future income (Benedictus et al., 1987; Kennedy and Benedictus, 2001). Using the “iceberg concept”, which states that for every animal with clinical signs of paratuberculosis in the herd, another 15–20 animals are *M. paratuberculosis*-infected (Whitlock et al., 2000), the cost of premature involuntary culling for the base herd of 100 cows was calculated to increase at a rate of US\$ 500 for every 20% (using 20 as the “iceberg factor”) rise in true prevalence, or US\$ 25 per infected cow in the herd.

In summary, the disease cost (DC) incurred while the infected cow is in the herd included decreased milk production, decreased fertility, increased mortality (replacement cost plus lost slaughter value), and increased premature involuntary culling as defined by the following equation:

$$\text{DC} = [\% \text{ milk reduction} \times \text{RHA} \times \text{milk price}/100] + \text{infertility costs} \\ + [(\text{RHC} + \text{SV}) \times \% \text{ mortality increase}] + \text{IC}$$

where SV = average weight of healthy cull cow  $\times$  slaughter price, RHA the rolling herd average, RHC the replacement heifer cost, and IC is the involuntary culling cost.

The disease cost was applied in the model for all infected cows remaining in the herd, i.e., those not culled (Fig. 2).

The value of the knowledge gained from all the true-negative test results was set as equal to the positive value of the DC (“+DC”) in a comparable herd (same size, infection prevalence, and herd hygiene level) that did not test for paratuberculosis, as in a previous decision tree (Collins and Morgan, 1991a). This value, +DC, was included in the cost formula for all test-negative cows that were truly not infected (Fig. 2).

Not all *M. paratuberculosis*-infected cows in a herd are at the same stage of infection. The impact of paratuberculosis on animal health and productivity is a direct function of stage of infection, and thus this factor needed to be incorporated into the model. The stages of *M. paratuberculosis* infection are typically defined by diagnostic test results, in

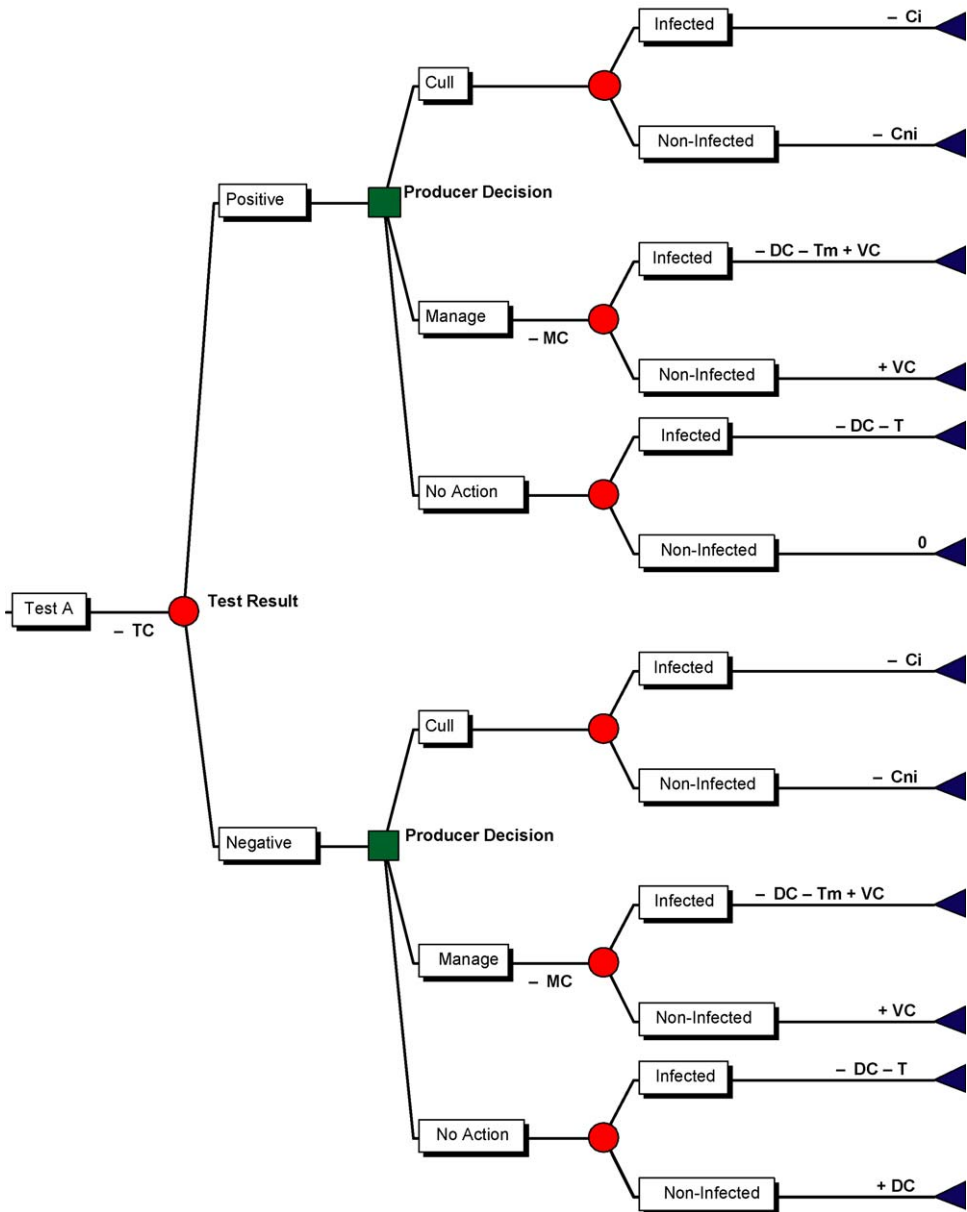


Fig. 2. Diagram of a portion of JD-Tree to show end node economic values.

particular the level of fecal shedding of *M. paratuberculosis* (Whitlock et al., 2000). ELISA results are correlated both with likelihood of and level of *M. paratuberculosis* shedding in feces (Sweeney et al., 1992, 1995; Whitlock et al., 2000; Collins, 2002; USDA, 2005). For the model, we assumed that cows in more advanced stages of *M. paratuberculosis* infection

were a greater cost to producers than cows in early infection stages. Infected cows with a “high” positive test result would, on average, have a greater economic impact than those with “moderate” positive level test results (regardless of test type). Likewise, cows with “moderate” positive results would cost more than “low” positives, and “low” positives would cost more than truly *M. paratuberculosis*-infected cows yielding a “negative” test result (false-negatives). To account for this, the average DC of each infected cow was calculated and then adjusted for each of the four diagnostic test classifications by multiplying the average DC times 1.5, 1.25, 0.75, and 0.5 for infected cows with high, moderate, low, and negative results, respectively. These multipliers are admittedly only rough approximations of the impact of disease stage, reflected in level of test results, on cost of Johne’s disease to producers.

### 2.3. Herd hygiene levels

Farm management practices directly affect the rate of *M. paratuberculosis* transmission. Improving these practices is the first priority of any on-farm paratuberculosis control plan. Reflecting this, the initial branch in the model was a decision node putting the producer into one of four herd hygiene (HH) levels based on current recommended calf management practices (Table 2). With these hygiene levels and

Table 2

Definition of herd hygiene levels, their estimated effect on *M. paratuberculosis* transmission, and annual costs to sustain this level of management

Management practice <sup>a</sup>	Herd hygiene level				Cost (US\$/cow/yr)
	HH-0	HH-1	HH-2	HH-3	
Feed hygienically collected colostrum from one cow to one calf	No	Yes	Yes	Yes	5.00 <sup>b</sup>
Feed milk replacer or pasteurized waste milk	No	Yes	Yes	Yes	22.50 <sup>c</sup>
Prevent contact of calves with adult cow manure	No	No	Yes	Yes	25.00 <sup>d</sup>
Improve maternity pen hygiene and sanitation	No	No	No	Yes	208.00 <sup>e</sup>
Estimated number of effective cow–calf contacts ( $k$ ) <sup>f</sup>	15.0	6.0	3.0	1.5	
Total cost (US\$/cow/yr)	0.00	27.50	52.50	260.50	

<sup>a</sup> All values are calculated assuming management practices are applied to heifer calves only and general farm labor is US\$ 10 h<sup>-1</sup>.

<sup>b</sup> Hygienic collection, preparation and feeding of colostrum from only one cow to one heifer calf. This assumes that some colostrum will be wasted and requires 1 h labor/calf/yr.

<sup>c</sup> This cost is based on feeding of milk replacer only. It assumes total exclusion of all waste milk, values milk replacer at US\$ 45/calf/yr, and assumes that the management change is from feeding of waste milk therefore the cost of replacer is not offset by increased profit from milk sales.

<sup>d</sup> Assumptions: requires use of calve hutches (US\$ 300 per calf) and super hutches (US\$ 750/5 calves), 5 calves use each hutch per year, and the hutches have a 10-year life span. This management practice may also include remodeling or building of new heifer housing facilities for heifers <1-year-old, purchasing separate equipment for feed and manure handling and extra labor associated with maintaining increased hygiene.

<sup>e</sup> Assumes one extra full-time employee at 40 h/week × US\$ 10 h<sup>-1</sup> to remove calves promptly, improve maternity pen hygiene and sanitation plus extra bedding costs.

<sup>f</sup> Effective cow–calf contacts reflect the effectiveness at preventing *M. paratuberculosis* transmission as defined in the paratuberculosis eradication model.



utilizing a paratuberculosis eradication model (Collins and Morgan, 1991b), the effect of the herd hygiene level on the number of effective cow–calf contacts ( $k$ ), and cost of implementing these herd management practices was established (Table 2). These assumptions and costs were validated by a group of paratuberculosis, dairy management, and production medicine experts (see Acknowledgments).

#### 2.4. Cost of new infections

A modified Reed–Frost equation was used to estimate the number of infected heifers raised on a farm based on the true within-herd prevalence. Reed–Frost equations were adapted (Collins and Morgan, 1991b) and modified to reflect the fact that not all *M. paratuberculosis*-infected cows are infectious. Diagnostic test sensitivity is a function of the spectrum of infection in the tested population (Ransohoff and Feinstein, 1978; Collins and Sockett, 1993). Stage 1 animals, prepatent (not yet shedding adequate numbers of *M. paratuberculosis* to be detectable by culture) and preclinical, represent an estimated 70% of all infected animals in a typical infected dairy herd (Whitlock et al., 2000). If one assumes animals shedding at undetectable levels are not infectious, then according to best estimates no more than 30% of all truly *M. paratuberculosis*-infected cows can be considered infectious. Thus, the number of infectious animals in a herd is 30% of the total number of infected individuals ( $I_a$ ). The annual calf crop was the susceptible population (i.e. 100% susceptible). The following equations were used to calculate the number of infected calves born in a given year that would eventually become replacements in the herd ( $I_r$ ):

$$I_r = (1 - (1 - p)^{I_a})(H \times R), \quad p = k/(H \times Br)$$

where  $p$  is the effective cow–calf contact rate,  $k$  the effective cow–calf contacts,  $H$  the herd size (number of milking adults  $\geq 2$  years of age),  $Br$  the annual birth rate in the herd and  $R$  is the annual herd replacement (culling) rate.

This quantity was expressed as the number of infected heifers raised per infected cow, a number used to establish infection transmission costs. A simplifying assumption throughout the model is that transmission costs per infected replacement that reaches the milking herd is equal to 1 year's lost milk production due to subclinical paratuberculosis plus impaired efficacy of testing and eradication strategies. Assuming that calving first occurs at 24 months then the annual cost of transmission incurred for each infected replacement reaching the milking herd expressed per infected cow per year is  $((1/2) \times \text{annual lost milk production})$ . For example, if a particular cow transmits the infection to two replacement heifers then the cost of transmission ( $T$ ) assigned to that cow is  $2 \times (1/2) \times \text{lost milk production}$ . In real terms for heifers with a ME305 of 9091 kg (20,000 lb) and milk at US\$ 0.26/kg (US\$ 12.00/100 lb) the cost for each heifer infected would be US\$ 94.54 [ $2 \times (1/2) \times (0.04 \times 9091) \times \text{US\$ } 0.26$ ]. This cost represents the lost investment by the producer to rear infected replacements, subsequent infection transmission perpetuating paratuberculosis on the farm, prolonged testing and eradication costs, and even lost opportunity for herd genetic improvement.

The herd hygiene level, described previously, is essentially a classification of the intimacy of contact between infectious cows and susceptible calves plus the general level

of hygiene in the calving pens and calf rearing facilities on the farm. Therefore, as the herd hygiene level increases, the number of effective cow–calf contacts ( $k$ ) decreases, resulting in fewer infected heifers raised per infected cow and thus a decrease in the costs associated with *M. paratuberculosis* transmission (Table 2). Although other modes of transmission are possible, the fecal–oral route is generally considered the most important (Kennedy and Benedictus, 2001). Reed–Frost equations were used only to gauge net on farm infection transmission rate for a given herd hygiene level and thereby estimate the cost of infection transmission. Hence the present decision analysis model is founded on the Reed–Frost principles of infection transmission but it is not intended to be an epidemic model.

## 2.5. Producer decisions (cull, manage, no action)

### 2.5.1. Cull a test-positive cow

While minimizing transmission risk is beneficial, culling is expensive for a producer. The cost difference between culling a *M. paratuberculosis*-infected (Ci) versus non-infected (Cni) cow has three components: reduced slaughter value (cost), a reduced herd life forcing greater investment in replacement animals (cost) (Kennedy and Benedictus, 2001) and avoided disease transmission (benefit). JD-Tree incorporates these values when a producer chooses to cull an animal from the herd (not to be confused with premature involuntary culling).

Slaughter values for infected cows were estimated by assuming that mean weight of infected cows when culled was 33.41 kg (73.5 lb) lower for every 10% increase in the within-herd prevalence (Johnson-Ifeorlundu et al., 1999). Healthy cows were assumed to weigh 681.8 kg (1500 lb). Cull cow values were set at US\$ 1.13/kg (US\$ 0.51/lb) (USDA Agricultural Prices Summary, July 2005, <http://usda.mannlib.cornell.edu/reports/nassr/price/zap-bb/agpran05.pdf>).

The cost of *M. paratuberculosis* transmission ( $T$ ) was avoided when truly infected cows were culled from the herd, an economic benefit not realized when a non-infected cow was culled. This is a simplifying assumption as some transmission events could have occurred prior to culling. It was assumed that infected cows stayed in the herd for a period 20% shorter than did uninfected cows. Replacement heifer price was set at US\$ 1500 (Wisconsin Agricultural Statistics Service, <http://www.nass.usda.gov/wi/>). Monthly ownership costs were computed using standard discounting techniques. Net present value was computed by subtracting the present slaughter value of a cow sold  $N$  months in the future from the initial cost of the cow (present value represents the net cost of acquiring the cow). Then, net present value was converted to a monthly cost, reflecting depreciation and the opportunity cost of capital, by dividing the net present value by the uniform present value factor for  $N$  months. The value obtained was the monthly charge for depreciation and capital over the useful life of the cow, which was then converted to an annual cost (assumes a 5% annual discount rate). Months per lactation was determined by subtracting 1.6 (assuming a 7-week dry period) from the calving interval, set at 14 months. The useful life of the cow was determined using a cull rate of 37% and a calving interval of 14 months to calculate the average number of lactations for a cow in the model herd as 2.317, i.e.,  $1/\text{cull rate} = \text{years in herd}$ , and  $\text{years in herd}/\text{calving interval} = \text{number of lactations before leaving the herd}$ . Using the aforementioned discounting techniques

applied to the replacement heifer cost less slaughter value, the annual depreciation for a non-infected and infected cow in the base herd was US\$ 310.40 and 390.39, respectively. As an example, a cow culled 1 year early results in losses of  $1 \times$  annual cost, and a cow culled 2 years early resulted in losses of  $2 \times$  annual cost. Assuming an average number of lactations in the herd and an equal temporal distribution of premature culling throughout the functional herd life, these values could be summed and averaged to find the average cost of premature voluntary culling.

It would be naïve to assume that culling a *M. paratuberculosis*-infected cow always resulted in replacement with an uninfected individual. A herd/regional replacement source classification was utilized to estimate the probability of purchasing an infected replacement heifer for the cow leaving the herd (Table 3). This was adapted from the Handbook for Vets and Dairy Producers, 6 pp., Table F (U.S. National Johne's Working Group, 2004) which is the basis for dairy herd risk assessment in the U.S. today. The model is only concerned with the risk of replacing the individual *M. paratuberculosis*-infected cow with another infected cow, taking into account the probability the source herd is infected, based on herd-level prevalence estimates, and the probability a cow within an infected herd is infected, i.e., within-herd prevalence. The net cost of purchasing an infected replacement was calculated by multiplying this probability by the cost of infection transmission, then adding the initial cost of purchasing the replacement heifer. Hence, buying a *M. paratuberculosis*-infected heifer was more costly than buying a noninfected heifer. For example if the replacement heifer source was classified as a "4", or a maximum risk source, there would be a 10% risk of purchasing an infected individual to replace the cow leaving the herd, and therefore 10% of the cost associated with transmission would be incurred.

### 2.5.2. Manage a test-positive cow

The producer's decision to "manage" a cow involves implementing effective herd management practices that reduce *M. paratuberculosis* transmission while retaining the cow in the herd, thus avoiding culling costs and maintaining profits from milk sales. These management practices include: permanently identifying cows, discarding the cow's colostrum and utilizing an alternative source of colostrum to feed the cow's calf (frozen

Table 3  
Replacement heifer source classification, description, and the estimated probabilities of a heifer from such source being *M. paratuberculosis*-infected

Classification	Description	Probability a heifer is <i>M. paratuberculosis</i> -infected <sup>a</sup>
1	VBJDHSP <sup>b</sup> levels 2–4 herd	0.0001
2	VBJDHSP level 1 herd or equivalent	0.001
3	Single source non-tested, non-program herd	0.01
4	Multiple untested source herds with no testing of purchased animals	0.1

<sup>a</sup> Assumptions based on experience and approximations of the probability the source herd is *M. paratuberculosis*-infected (estimated herd prevalence) and the probability a cow from the herd is infected (estimated within-herd prevalence).

<sup>b</sup> U.S. Voluntary Bovine Johne's Disease Herd Status Program.

from test-negative cow, artificial replacement products, etc.), discarding all waste milk from the cow, immediately (within 0.5 h) removing a calf born to the cow from the calving area, use of a separate maternity pen dedicated to only test-positive cows, not breeding test-positive cows, and culling of such cows from the herd within 12 months of the positive test result. At this level of test-positive cow management, the “manage” branch at the producer decision node resulted in a lower cost of infection transmission ( $T_m$  = transmission cost-managed) for infected cows as compared to infected cows not managed in a herd of the same herd hygiene level.

The model includes an input variable called cow management factor (CMF) to account for infected cows management costs and that not all herd managers would be equally effective in managing *M. paratuberculosis*-infected cows. The CMF ranked the ability of the producer to manage test-positive cows as excellent, average, or poor, and these then translated to a 75%, 50%, or 25% reduction in “ $k$ ” (effective cow–calf contact) at costs per cow of US\$ 30, 15, and 5, respectively. These are assumptions since no published evidence on the extent to which CMF might alter “ $k$ ” could be found. The “manage” branch only reduces disease transmission costs; the disease cost (DC, e.g. decreased milk production and reduced fertility) for infected cows is fully realized when an infected cow is retained in the herd.

A producer decision to manage a test-positive cow was assumed to result in lower veterinary costs (estimated to be one-half normal investment in veterinary medications and treatments) since producers typically avoid investing money to solve other health problems in a paratuberculosis test-positive cow. The average veterinary costs per cow per year was set at US\$ 0.924/100 kg (US\$ 0.42/100 lb) (Frank and Vanderlin, UW Center for Dairy Profitability. 2003. <http://cdp.wisc.edu/pdf/02cost.pdf>). The cost of voluntary culling ( $C_i$  and  $C_{ni}$ ) was recovered in the model if a test-positive animal was retained in the herd and managed because it allows the producer to continue to selectively cull other animals and to capture what would otherwise be lost future income from that specific cow.

### 2.5.3. Take no action on a test-positive cow

The cost of transmission and cost of disease were fully incurred for truly *M. paratuberculosis*-infected cows if “no action” was taken at the producer decision node. The economic cost of taking no action with tested and true-negative cows was represented by the positive value of the cost of disease in a herd of the same size, prevalence, and herd hygiene level but not testing for paratuberculosis. For cows with false-positive test results this positive economic value was not received because they were misdiagnoses.

### 2.6. Test parameters and costs

Test accuracy parameters are based on field studies (Collins et al., 2005) and test costs are based on charges currently levied by approved paratuberculosis testing laboratories in the U.S. time, labor, shipping and handling, and other sampling expenses of the veterinarian, herd manager, and any other workers have been estimated for each test and included in the model in order to make test cost a more accurate representation of the actual producer cost of testing (Table 4).

Table 4

Characteristics of five diagnostic tests for paratuberculosis used in the model with the likelihood ratio for each test and level of test result

Test	Cost per cow (US\$)	Result level	Percent infected cows with result (true-positive rate)	Percent noninfected cows with result (false-positive rate)	Likelihood ratio
A	10.00	High	0.1759	0.0028	63.149
		Moderate	0.0627	0.0056	11.246
		Low	0.0506	0.0334	1.514
		Negative	0.7108	0.9582	0.742
B	5.00	High	0.1343	0.0001	1342.926
		Moderate	0.1511	0.0028	54.253
		Low	0.0552	0.0195	2.829
		Negative	0.6595	0.9776	0.675
C	20.00	High	0.1936	0.0001	1936.000
		Moderate	0.1686	0.0001	1686.000
		Low	0.1185	0.0100	118.500
		Negative	0.5193	0.9988	0.520
D	25.00	High	0.1651	0.0001	1651.000
		Moderate	0.0304	0.0001	304.000
		Low	0.0209	0.0010	20.900
		Negative	0.7836	0.9988	0.785
E	20.00	High	0.1435	0.0001	1435.000
		Moderate	0.1754	0.0001	1754.000
		Low	0.0456	0.0010	45.600
		Negative	0.6355	0.9988	0.636

## 2.7. Diagnostic test probabilities

### 2.7.1. Multi-level interpretation of diagnostic tests (high, moderate, low, and negative)

Decision analysis requires the use of probabilities at chance nodes in the tree. These are the “test result” and “true infection state” chance nodes in our model. For the test result node, the proportion of cows yielding a given level of test result, apparent prevalence (AP), for each of five different types of tests was derived from field studies where nine diagnostic tests were applied to 2453 cows (Collins et al., 2005). The AP was used together with the true within-herd prevalence (TP) input variable to determine the proportion of cows in each branch of the test result node (five tests  $\times$  four test result levels).

The final chance node in the decision tree was the true *M. paratuberculosis* infection state node (infected or noninfected). Probability estimates for this node were determined using likelihood ratios (LR) (Sackett et al., 1991). The LRs were derived from field study data reported previously (Collins et al., 2005). Standard methods were used to convert true prevalence (input variable) to pre-test odds of infection which, when multiplied by the appropriate  $LR^+$ , gave the post-test odds of infection that were then converted to a post-test infection probability. This system was applied throughout the

model with the respective  $LR^+$  for each specific test and each test result level (Table 4). The summary equations are:

post-test probability positive

$$= [(TP/(1 - TP)) \times LR^+]/[1 + (TP/(1 - TP)) \times LR^+]$$

where TP is the true prevalence and  $LR^+$  is the likelihood ratio for a positive test. Post-test probability negative ( $LR^-$ ) is  $(1 - \text{post-test probability positive})$ . It should be noted that the more common Bayes form of equations used for dichotomous test interpretation produces the same results, i.e., predictive value of a positive (PVP) =  $(\text{prev} \times \text{Se})/(\text{prev} \times \text{Se}) + (1 - \text{prev}) \times (1 - \text{Sp})$ , where prev is the true prevalence, Se the sensitivity and Sp is the specificity.

For organism detection-based diagnostic tests such as fecal culture on the conventional, solid agar medium Herrold's Egg Yolk Agar (Test C), direct fecal PCR (Test D) or culture in liquid medium such as modified BACTEC 12B medium (Test E), LR calculation was problematic due to incorporation bias. That is, the test itself was used to define which animals were infected or non-infected in field studies, creating a circular definition and implying that culture is a perfect diagnostic assay that never errs when positive. This is problematic for LR calculations in that culture-positive animals would, by definition, never be found in a non-infected population. Hence, for all four levels of a positive culture test result the denominator would be zero making the LR infinitely high. While a high positive culture result (3+ or 4+ fecal shedding level), or even a moderate positive (2+) culture result, would likely never be considered false-positive, a low positive (1+) result, potentially representing just 1 colony on a single slant of four inoculated HEY slants, might be questioned as valid by some diagnosticians because of the potential for "pass through", that is ingestion and passage of *M. paratuberculosis* through the intestinal tract without the animal being truly infected. To handle the mathematical problem of dividing by zero and acknowledge the rarity of an incorrect diagnosis when moderate- or high-positive culture or PCR results are obtained, the following proportions of truly non-infected animals yielding such results were adopted as a convention for both culture-based and PCR-based tests: high level result (0.0001), moderate level result (0.0001) and low level result (0.001).

## 2.8. Analysis of model outcomes

By a process known as "averaging out and folding back" the PrecisionTree<sup>®</sup> program determined the economically optimal path in the decision tree resulting in a so-called "policy suggestion". This was done by calculating the expected value of the furthest right-hand chance nodes and reducing them to a single event by multiplying the probability at each branch by the appropriate final path value and then summing economic outcomes for each chance node. This formed a weighted average value for each chance node. The optimum path of the right-hand decision nodes was chosen and reduced to a single event. This then was repeated until all nodes had been analyzed. In this way, the program determined the optimal path from the 960 possible path choices using producer economics as the measure of what was the "best control program", i.e., the policy suggestion.

Table 5

Model input variable and the ranges used for each when performing sensitivity analyses<sup>a</sup>

Input variable	Base	Minimum	Maximum
Herd size (no. of milking adult cows)	100	50	3000
Infection prevalence (true prevalence)	0.10	0.001	0.35
RHA; kg milk (lb milk)	9759 (21470)	5455 (12000)	13636 (30000)
Milk price; US\$/kg (US\$/100 lb)	US\$ 0.275 (US\$ 12.50)	US\$ 0.198 (US\$ 9.00)	US\$ 0.55 (US\$ 25.00)
Replacement heifer cost; US\$	US\$ 1500	US\$ 1000	US\$ 2500
Slaughter value of culls; US\$/kg live weight (US\$/100 lb live weight)	US\$ 1.034 (US\$ 47.00)	US\$ 0.858 (US\$ 39.00)	US\$ 1.232 (US\$ 56.00)
Birth rate	0.86	0.70	0.95
Calving interval; months	14	13	15
Replacement rate	0.37	0.25	0.45
Effect of JD on milk production (% reduction ME305)	4	1	15
Cow management factor	2	1	3
Replacement source	2	1	4

<sup>a</sup> Only the results of sensitivity analyses showing significant affects on model outcomes are reported in this publication.

The base herd was constructed using variables chosen to represent a typical Midwest U.S. commercial dairy herd (Table 1). Sensitivity analysis was then performed by holding all values in the model constant except 1 (one-way analysis) or 2 (two-way analysis) that were varied using values in reasonable ranges (Table 5). Such analyses determined which input variables had little impact on the outcome, and these then were treated as deterministic and set to their base herd values. Variables that strongly influenced model outcomes and interacted with other model variables were evaluated by two-way sensitivity analysis with the aid of strategy region graphs (SRG).

The PrecisionTree<sup>®</sup> program reports two-way sensitivity analysis for any pair of selected variables based on their impact on a specific branch in the decision tree. To contrast how these two variables affected different pathways in the tree required doing two-way sensitivity analyses on multiple tree branches and combining the results to create composite SRGs. All SRGs shown in this report are composites and these SRGs are used to describe most of the model variable interactions. To interpret a SRG one finds two coordinates describing a specific farm, e.g., herd size and infection prevalence, and uses these coordinates to locate the region of the graph where they intersect. The legend for that graph region then explains what type of control program (strategy) is optimal for a herd of such characteristics. The model also can display the results as three-dimensional graphs where the third, Z, axis is the net economic impact of the various combinations of herd characteristics.

### 3. Results

#### 3.1. Net cost of paratuberculosis and paratuberculosis control: base herd

In JD-Tree, the costs of paratuberculosis to a dairy producer increase as the prevalence of *M. paratuberculosis* infections in the dairy herd increases. Implementation of a control



program reduces these losses. For the 100 cow base herd (Table 1), the model predicts losses attributed to paratuberculosis of US\$ 156 and 122 per cow per year for herds that are not testing and testing, respectively. It is important to note that these values represent a best case scenario because they assume the consistent performance of herd hygiene recommendations and consistent and appropriate actions on diagnostic test results, i.e., consecutive branches in the optimal decision tree path are not independent. Consequently, the cost estimates should be considered the minimal economic losses attributed to the given control strategy. These losses will be greater if a producer is not correctly and consistently employing the most economical combination of decisions. While the costs of paratuberculosis found in the model are in the range of values reported from field studies (Ott et al., 1999), results reported by JD-Tree are best used to reveal trends and interactions and should not be interpreted as absolute monetary losses or gains. The financial results instead are designed to signal the most economically attractive paratuberculosis control program.

### 3.2. Policy suggestion for the base herd

JD-Tree shows that the economically favorable paratuberculosis control program for the base herd includes managing the herd at HH-1 and regular herd testing with Test B, the milk ELISA (Fig. 3). The model further recommends culling cows that test moderate- or high-positive and managing cows with low-positive results. Obviously, taking no action was recommended for test-negative cows. Subsequent analyses explore how specific input variables affected this policy suggestion for the base herd. For all scenarios, the optimal outcome is based exclusively on farm economics for the subsequent 12-month period.

### 3.3. Sensitivity analysis on all input variables

PrecisionTree<sup>®</sup> calculates the impact of each model variable at any selected node in the decision tree and displays this graphically as a Tornado Diagram. At the root of the tree (net economic impact of all tree branches) the input variables with the greatest effect on model outcome (percentage change from base value) were in decreasing order; within-herd prevalence, milk price, RHA, effect of paratuberculosis on milk production, herd replacement rate, herd size, replacement heifer cost, diagnostic tests costs and herd birth rate (Fig. 4). Compared to the second most influential variable, milk price, the within-herd infection prevalence had approximately five times greater impact on the net economic impact JD-Tree results.

### 3.4. Factors affecting decisions at the herd hygiene node

HH-1 was optimal for the base herd. Implementing HH-3 was cost prohibitive for the herds of 100 cows, however, one-way sensitivity analysis revealed that as the herd size increases, management of herds at HH-3 becomes more favorable with HH-3 being the policy suggestion advisable for herds of >850 cows (Fig. 5). JD-Tree also concludes that as within-herd prevalence increases it becomes progressively more favorable to implement more intensive herd hygiene as the least cost method of paratuberculosis control (Fig. 6).



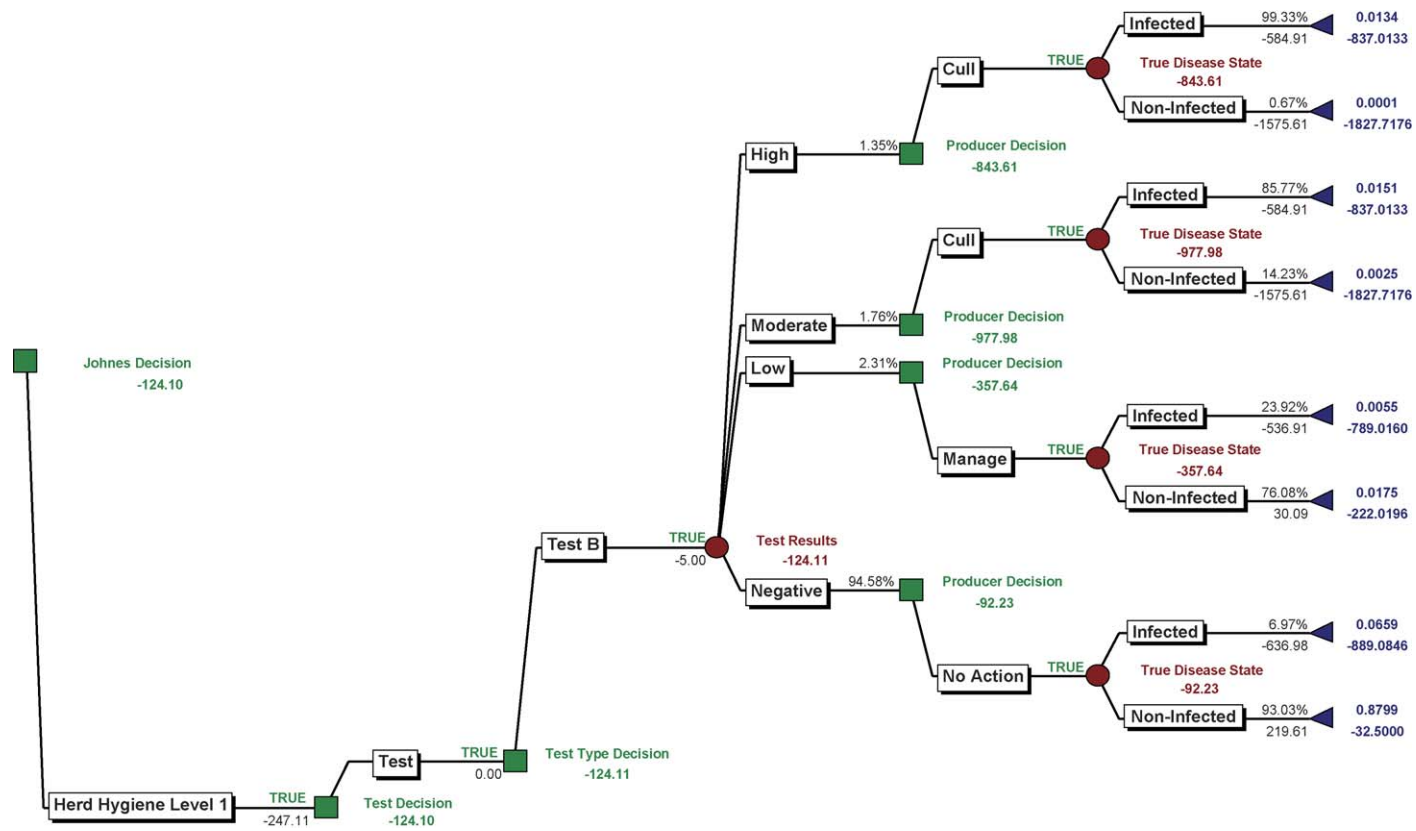


Fig. 3. Policy decision result for the base herd. The optimal decision path for all possible outcomes is shown along with the net economic impact at each end node.

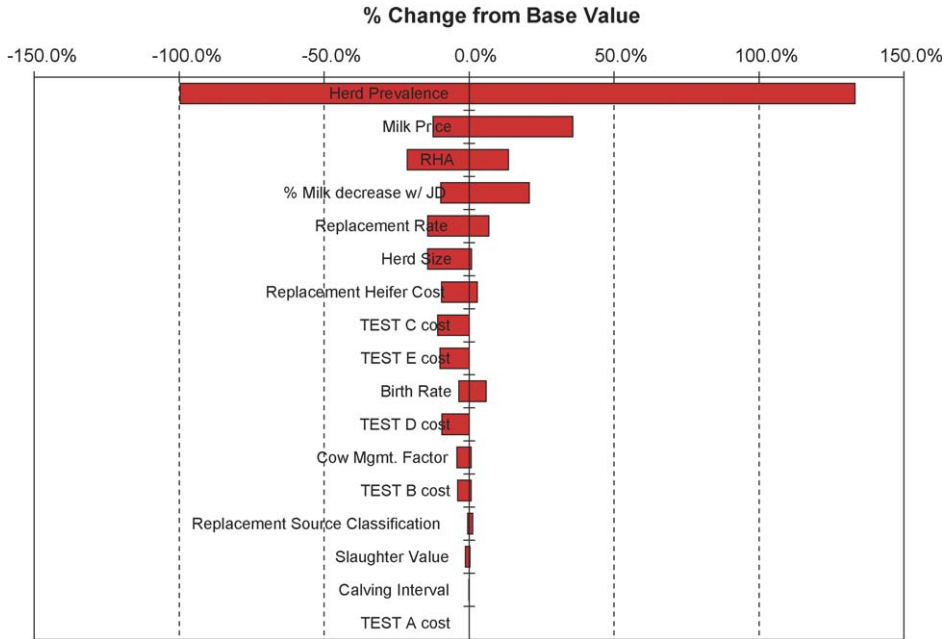


Fig. 4. Tornado diagram showing impact, and percent change from base value, of all major input variables on the net model outcome.

### 3.5. Factors affecting decisions at the test decision node

JD-Tree found that some sort of testing is almost always an economically justifiable component of a paratuberculosis control program for the base herd. In fact, unless the within-herd infection prevalence is <0.5%, testing is always an economically better decision than not testing. From 0.5% to 4.25% prevalence the best action becomes testing and managing at HH-0, from 4.25% to 12.0% prevalence, testing and managing at HH-1, and from 12.0% to 35.0% prevalence testing and managing at HH-2 is economically most favorable. The model indicates that even herds of >1000 cows should include testing in their control program, unless they maintain an exceptional herd hygiene level (HH-3).

### 3.6. Factors affecting decisions at the test type decision node

The model evaluates the cost of diagnostic tests together with test accuracy and assumes that producers pay fair market price for each test, including veterinary fees for sample collection. For the base herd, the model found that Test B was most often the best test (highest cost–benefit). Test B has the characteristics of a commercially available milk ELISA for individual cow milk samples (not bulk tank). The ranked order of tests (most to least cost-effective) was B, C, E, A, and D. Test B remained the test of choice up to a price of roughly US\$ 12.00 per cow (data not shown). Sensitivity analysis showed that of the test

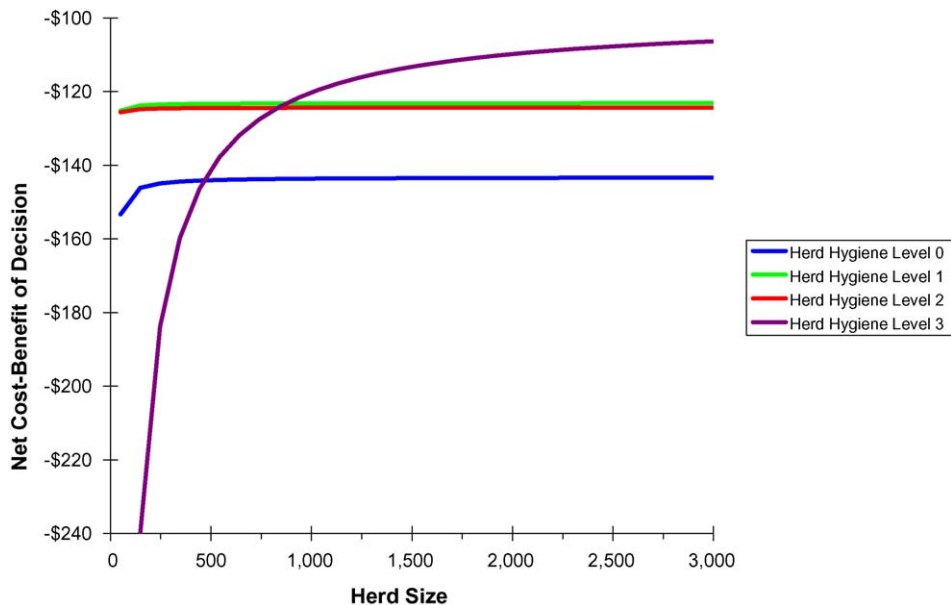


Fig. 5. One-way sensitivity analysis of herd size. Comparison of the impact of herd size on the benefit–cost of a paratuberculosis control program in dairy herds managed at each of four hygiene levels (with all other variables held constant at baseline values). This graph shows that it is economically optimal for large herds (>1000 cows) with a 10% within-herd prevalence to operate at hygiene level 3.

parameters included in the model, test cost and sensitivity for detecting cows in advanced stages of paratuberculosis were most influential for test selection.

### 3.7. Factors affecting decisions at the producer actions on test results node

Optimal producer decisions based on test results are significantly affected by herd hygiene level, test type, and level of test result (Table 6). At higher herd hygiene levels, HH-2 and HH-3, the optimal producer decision is most often to manage the test-positive cow as opposed to culling it or taking no action. At HH-0, and HH-1 the optimal decision tended more often to be culling of cows, in particular those with high-positive test results. This reflects the ability of the producer to limit *M. paratuberculosis* transmission through herd management and the economic advantages of keeping the cow in the herd longer to generate more farm income. For tests C, D and E culling test-positive cows was more often the recommended producer action for multiple test result levels. Tests C, D, and E are organism detection-based tests in use today. Because of their high specificity these tests have a high likelihood of correct identification (diagnosis) of infectious cows (Table 4).

### 3.8. Two-way sensitivity analysis on high impact variables

Two-way sensitivity analysis was performed for all the variables in the model, however, the interactions of only the four variables with the greatest impact on model outcomes

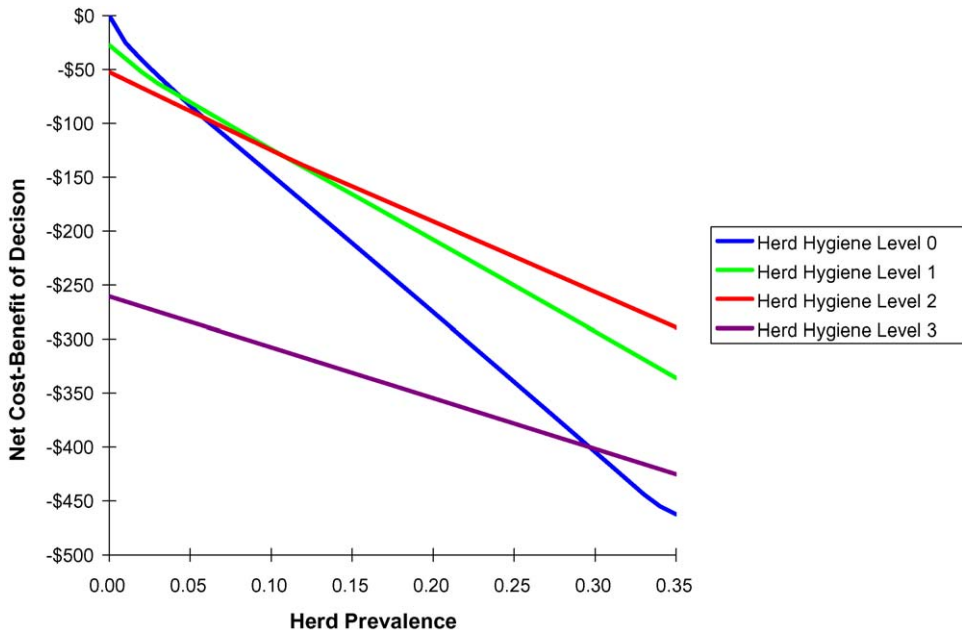


Fig. 6. One-way sensitivity analysis of herd prevalence. Comparison of the impact of within-herd *M. paratuberculosis* infection prevalence on the benefit–cost of a paratuberculosis control program for the baseline dairy herd managed at each of four hygiene levels (with all other model variables held constant and at baseline values). The upper-most line at any level of prevalence is the economically optimal herd hygiene level for paratuberculosis control. The optimal hygiene level changes with prevalence but for the baseline 100 cow dairy herd with 10% prevalence operation at hygiene level 3 is never economically optional.

are presented here. These two-way strategy region graphs (SRGs) indicate the most economically favorable (“best”) paratuberculosis control program, as defined by JD-Tree, while simultaneously varying two herd characteristics. SRGs allow a more complete understanding of how farm-specific factors affect the design of cost-effective paratuberculosis control programs.

### 3.9. Herd size and within-herd infection prevalence interaction

The interaction of herd size, from 0 to 3000 cows, and within-herd *M. paratuberculosis* infection prevalence, from 0.0% to 35% shows five different regions on the SRG denoted by different colors (Fig. 7). Each of these regions represents a different economically optimal paratuberculosis control program. The recommendation for noninfected herds of any size is not to implement herd hygiene changes nor do any testing (green region). In all subsequent SRGs the same model recommendation is made: in the absence of infection no paratuberculosis control program is needed, hence it will not be mentioned when describing the remaining SRGs. When within-herd infection prevalence is >0.5% the model advises all herds to have some form of paratuberculosis control program: herds of any size with <5% infection prevalence need only use Test B and make no management changes (red region);

Table 6

Optimal producer decisions reported by the JD-Tree model for the base herd stratified by herd hygiene level, test type, and test result

Test	Result	Herd hygiene level			
		HH-0	HH-1	HH-2	HH-3
A	High	Cull	Cull	Manage	Manage
	Moderate	Manage	Manage	Manage	Manage
	Low	Manage	Manage	Manage	Manage
	Negative	No action	No action	No action	No action
B	High	Cull	Cull	Cull	Manage
	Moderate	Cull	Cull	Manage	Manage
	Low	Manage	Manage	Manage	Manage
	Negative	No action	No action	No action	No action
C	High	Cull	Cull	Cull	Manage
	Moderate	Cull	Cull	Manage	Manage
	Low	Cull	Manage	Manage	Manage
	Negative	No action	No action	No action	No action
D	High	Cull	Cull	Cull	Manage
	Moderate	Cull	Cull	Manage	Manage
	Low	Manage	Manage	Manage	Manage
	Negative	No action	No action	No action	No action
E	High	Cull	Cull	Cull	Manage
	Moderate	Cull	Cull	Manage	Manage
	Low	Cull	Manage	Manage	Manage
	Negative	No action	No action	No action	No action

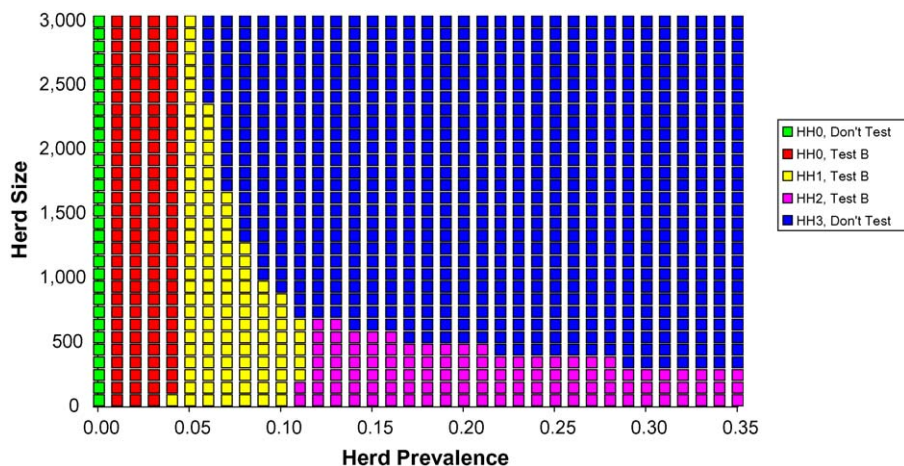


Fig. 7. Two-way sensitivity analysis composite strategy region graph of herd size and herd prevalence. The color found at the intersection of a specific herd size and specific within-herd infection prevalence defines the economically optimal paratuberculosis control program herd hygiene (HH) level and diagnostic test (with all other model variables held constant and at baseline values). Test B has the characteristics of a milk ELISA (ELISA for serum antibodies to *M. paratuberculosis* performed on milk samples).

herds with roughly 5–10% prevalence, depending on size, should operate at HH-1 and use Test B to detect infected cows (yellow region); herds of roughly 500 cows or less and >10% prevalence should operate at HH-2 and use Test B (purple region); and herds of >500 cows and prevalence >10% should operate at HH-3 and do no testing (blue region).

### 3.10. Milk price and within-herd prevalence interaction

In the face of low milk prices, not testing for paratuberculosis is an economically viable strategy under certain situations. The SRG of milk price and prevalence interactions shows that for the base herd at a milk price of US\$ 0.198/kg (US\$ 9.00/100 lb), managing at HH-2 and not testing is the economically optimal paratuberculosis control decision when infection rates are roughly 11–25% (Fig. 8; red region). At prevalence of 2–5%, the model recommends management at HH-0 and use of the lowest cost Test B (yellow region) or Test C (brown region), depending on milk price. When prevalence is 5–10% the model recommends improving herd management to HH-1 and using Test B (purple region) or Test C (light blue region). When milk prices is US\$ >0.264/kg (US\$ 12/100 lb) and prevalence is >10% managing at HH-2 and using Test B is generally recommended (blue region). Regardless of milk price or herd prevalence combination, the highest herd hygiene level, HH-3, was never advised as part of the optimal paratuberculosis control program for the 100 cow base herd.

### 3.11. Herd productivity and within-herd prevalence interaction

As one might expect, the RHA–prevalence SRG (Fig. 9) resembles that for milk price and prevalence since both RHA and milk price reflect farm income and thus the capacity

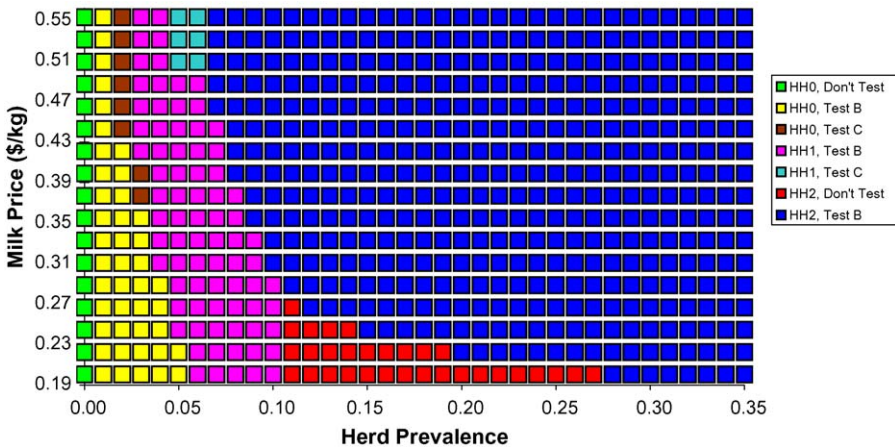


Fig. 8. Two-way sensitivity analysis composite strategy region graph of milk price (US\$/kg) and herd prevalence. The color found at the intersection of a specific milk price and specific within-herd infection prevalence defines the economically optimal paratuberculosis control program herd hygiene (HH) level and diagnostic test (with all other model variables held constant and at baseline values). Test B has the characteristics of a milk ELISA (ELISA for serum antibodies to *M. paratuberculosis* performed on milk samples). Test C has the characteristics of conventional fecal culture for *M. paratuberculosis* on solid agar media.



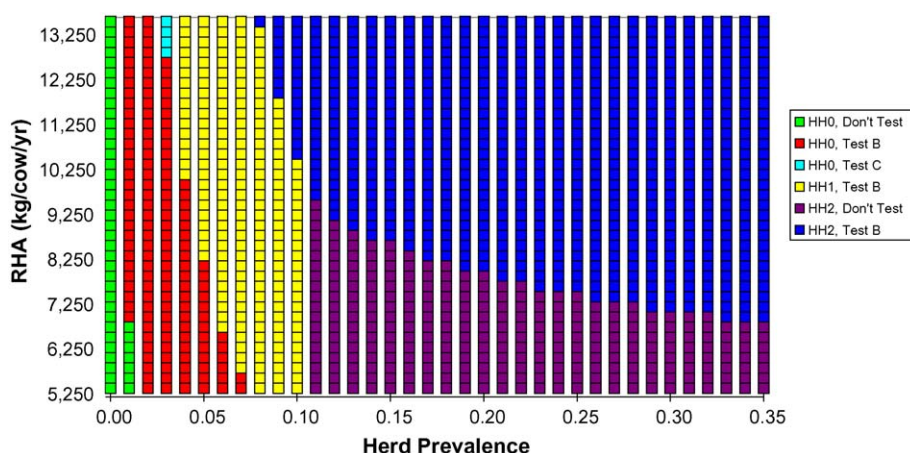


Fig. 9. Two-way sensitivity analysis composite strategy region graph of herd productivity (kg/cow/yr) and within-herd infection prevalence. The color found at the intersection of a specific level of herd productivity and specific within-herd infection prevalence defines the economically optimal paratuberculosis control program herd hygiene (HH) level and diagnostic test (with all other model variables held constant and at baseline values). Test B has the characteristics of a milk ELISA (ELISA for serum antibodies to *M. paratuberculosis* performed on milk samples). Test C has the characteristics of conventional fecal culture for *M. paratuberculosis* on solid agar media.

of the herd owner to invest in paratuberculosis control. As both the RHA and prevalence increase, higher herd hygiene levels are advised for the base 100 cow herd. Testing was the economically best option when combined with management at HH-2 for herds like the base herd if the herd's RHA was roughly >9090 kg/cow/yr (>20,000 lb/cow/yr) and herd prevalence was roughly greater than 10% (blue region). Test C (conventional fecal culture) was only advised for low prevalence herds (3%) when the herd RHA was high (>11,818 kg/cow/yr, or >26,000 lb/cow/year) reflecting this test's high sensitivity and higher cost (light blue region).

### 3.12. Milk price and herd productivity interactions

For the base herd, variations in milk price and RHA produced four paratuberculosis program recommendations (Fig. 10). Herds with low RHA in the face of low milk prices should manage at HH-1 and not test for paratuberculosis (yellow region). When the combination of milk price and RHA provides modest farm income, the model recommends managing at HH-1 and testing using Test B (green region). When economic conditions are even better (good milk price–RHA combinations) the model indicates herds should manage at HH-2 and test using Text B (blue region). Only at the best possible combination of milk price and RHA was Test C recommended (red region).

### 3.13. Milk price and herd size interaction

Interaction of milk price and herd size for herds with 10% infection prevalence produced an SRG with three main regions (Fig. 11). In general, the model recommends that

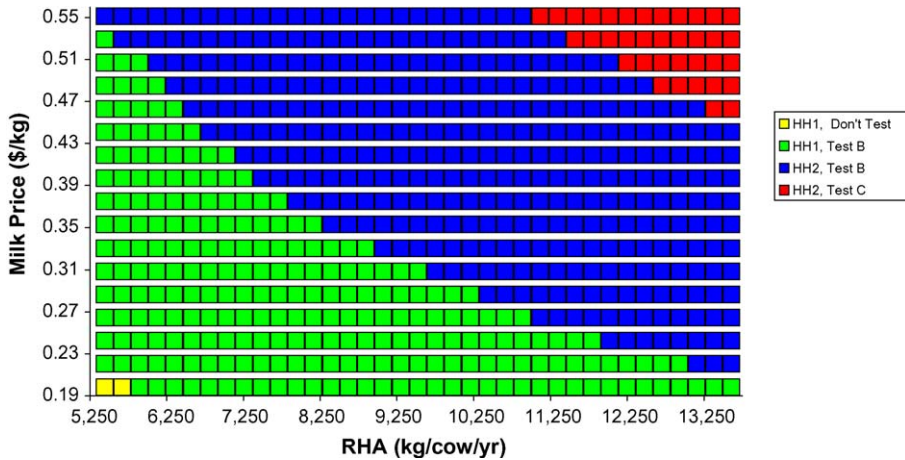


Fig. 10. Two-way sensitivity analysis composite strategy region graph of milk price (US\$/kg) and herd productivity (kg/cow/yr). The color found at the intersection of a specific milk price and level of herd productivity defines the economically optimal paratuberculosis control program herd hygiene (HH) level and diagnostic test (with all other model variables held constant and at baseline values). Test B has the characteristics of a milk ELISA (ELISA for serum antibodies to *M. paratuberculosis* performed on milk samples). Test C has the characteristics of conventional fecal culture for *M. paratuberculosis* on solid agar media.

herds of >750 cows manage at HH-3 and not test for paratuberculosis (blue region). Smaller herds should manage at HH-1 when milk prices are US\$ <0.31/kg (US\$ <14.00/100 lb) (yellow region) and at HH-2 when milk prices are US\$ >0.31/kg (red region) while also using Test B.

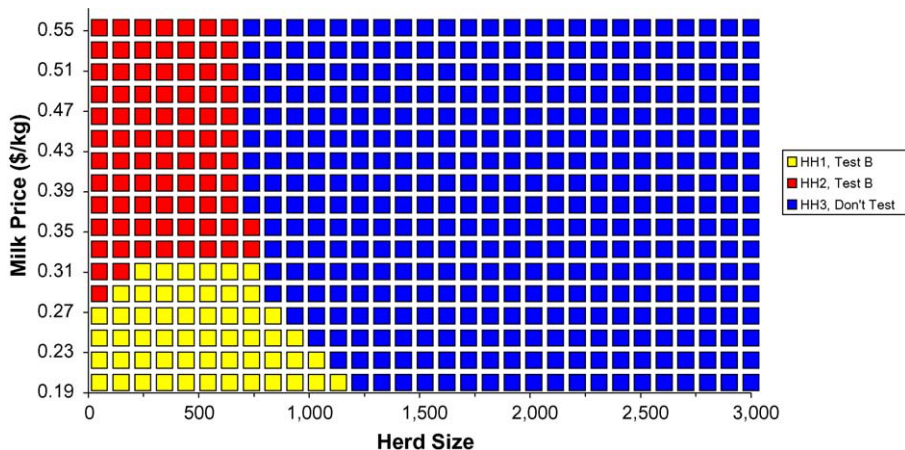


Fig. 11. Two-way sensitivity analysis composite strategy region graph of milk price (US\$/kg) and herd size. The color found at the intersection of a specific milk price and herd size defines the economically optimal paratuberculosis control program herd hygiene (HH) level and diagnostic test (with all other model variables held constant and at baseline values). Test B has the characteristics of a milk ELISA (ELISA for serum antibodies to *M. paratuberculosis* performed on milk samples).



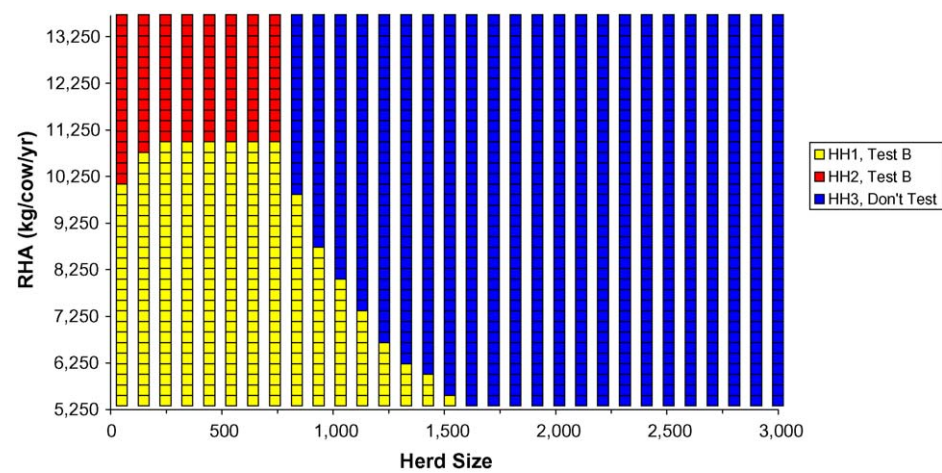


Fig. 12. Two-way sensitivity analysis composite strategy region graph of herd productivity (kg/cow/yr) and herd size. The color found at the intersection of a productivity level and specific herd size defines the economically optimal paratuberculosis control program herd hygiene (HH) level and diagnostic test (with all other model variables held constant and at baseline values). Test B has the characteristics of a milk ELISA (ELISA for serum antibodies to *M. paratuberculosis* performed on milk samples).

3.13.1. Herd productivity and herd size interactions

Interactions of RHA and herd size, for herds with 10% infection prevalence, also produced an SRG with three main regions (Fig. 12). In general, the model recommends that herds of <1000 cows with an RHA of <10,909 kg/cow/yr (<24,000 lb/cow/yr) should use the lower cost paratuberculosis control program, i.e., manage at HH-1 and use Test B (yellow region). Herds of 800 or less cows with very high production (>10,909 kg/cow/yr) should manage at HH-2 and use Test B (red region). And, as indicated in other SRG analyses, in general large herds (>1000 cows) with 10% infection prevalence at most any RHA should manage at the highest level of hygiene, HH-3, but not test to control paratuberculosis (blue region).

3.13.2. Test cost and test accuracy

Test cost is an influential model input variable (Table 7). When set to base values of US\$ 10, 5, 20, 25, and 20 for Tests A, B, C, D, and E, respectively (estimated non-subsidized

Table 7  
The impact of test cost on JD-Tree recommendations for the optimal test for use in a paratuberculosis control program

Scenario	Cost (US\$) for each type of test					Recommendation		Action on results: C = cull and M = manage		
	A	B	C	D	E	HH	Test	Low	Mod	High
A	10	5	20	25	20	1	B	M	C	C
B	10	10	10	10	10	1	C	M	C	C
C	15	15	15	15	15	2	No test	–	–	–
D	5	5	15	15	15	1	B	M	C	C

costs for serum ELISA, milk ELISA, conventional fecal culture, direct fecal PCR, and fecal culture in liquid media), the JD-Tree policy suggestion for the base herd is to manage the herd at HH-1 and use Test B for paratuberculosis control. By contrast, if all tests are US\$ 10, the optimal control program is management at HH-1 and use of Test C (conventional fecal culture) followed by culling of moderate and high-positive cows and management of cows with low-positive test results. If the cost of all tests is set to US\$ 15, the policy suggestion is to not use paratuberculosis tests at all but rather to manage the herd at HH-2 to control paratuberculosis. If antibody detection-based tests A and B are priced at US\$ 5 and the three organism detection-based tests are priced three times higher at US\$ 15, the best program for the base herd is again to manage at HH-1 and use Test B, then cull the moderate and high-positive cows and manage cows with low-positive test results. If the exact same scenario is used but the herd size is changed to 1000 cows, the policy suggestion becomes to manage at HH-3 and not use paratuberculosis tests (data not shown).

#### 4. Discussion

The forerunner decision tree of JD-Tree (Collins and Morgan, 1991a) was built to evaluate a single diagnostic test for paratuberculosis, interpreted only as positive or negative, and used to make the decision whether to keep or cull dairy cattle. It concluded that testing and culling test-positive cattle was not cost-effective unless the prevalence of *M. paratuberculosis* infection in the herd exceeded 5%.

JD-Tree expands on producer options to include both management changes and testing to suggest the most cost-effective paratuberculosis control program. It includes more economic parameters and uses new software tools allowing examination of interactions among variables in the model. JD-Tree includes disease transmission components similar to the epidemic models of Collins and Morgan (1991a,b) and Groenendaal and Galligan (2003), but primarily for the purpose of estimating the costs associated with transmission of *M. paratuberculosis* infection to replacement heifers. The model determines the economically optimal paratuberculosis control program for commercial dairy producers. Unique to JD-Tree is the inclusion of a decision node allowing the model to “select” any one of five diagnostic tests. Each test has accuracy and cost inputs based on published field trial data. Additionally, JD-Tree employs likelihood ratios to compute post-test probabilities of *M. paratuberculosis* infection for four levels of test result for each of the five tests.

JD-Tree includes best possible estimates of the costs of paratuberculosis control based on implementation of critical farm management practices targeted at limiting infection transmission. The costs of paratuberculosis control are balanced against the benefits of controlling the infection using published estimates of the cost of paratuberculosis in dairy herds. For herds of 100 cows with a 10% *M. paratuberculosis* infection true prevalence, managing at the lowest hygiene level, HH-1, and not testing, the cost of paratuberculosis is estimated at US\$ 156 per cow in the herd/year, close to the costs estimated in field studies in the US (Ott et al., 1999). By simply improving calf-hygiene and operating at HH-2, that cost could be reduced to US\$ 122 per cow in the herd/year. These values represent a best

case scenario because they assume the inclusion of every optimal decision in the tree including appropriate actions taken on diagnostic test results. Cost estimates should be considered the minimal economic losses attributed to the given control strategy. These losses will be greater if a producer is not correctly employing the most economical combination of decisions.

JD-Tree does not account for the reduction of economic losses due to other diseases resulting from improved herd management as part of the paratuberculosis control program, so-called “integrated disease control”. It is likely that if this were incorporated into the model, many of the herd hygiene decisions would become more favorable by cost sharing with other disease control programs.

Infection prevalence within-herd is the most important input variable in the JD-Tree model. This highlights the importance of accurate estimation of within-herd *M. paratuberculosis* infection rates, a vital part of on-farm risk assessment. Test B is economically the most favorable test because of its combination of low cost and high sensitivity, especially for “high” test results. The frequency of truly infected cows versus truly noninfected cows yielding this level of test result provides the likelihood ratio which has a large influence in the model. The influence of the LR is compounded because the cost of paratuberculosis for these high-positive cows is greater than for all the other diagnostic test levels. These cows with late stage *M. paratuberculosis* infections are most important in perpetuating the epidemic in the herd and also the most expensive when they are not detected (false-negative test results).

Larger herds can better afford to implement herd hygiene level 3 because management costs are relatively fixed whether the farms size is 100 or 3000 cows. These costs are therefore divided over more cows in the herd resulting in a lower cost per cow of implementing HH-3 for larger herds. It appears that for larger herds that can better afford to operate at herd hygiene level 3, the additional improvements in hygiene replaces the need for diagnostic testing. This is logical in that rigorous infection control through hygiene could reduce the probability of infection transmission events to near zero and the obligate pathogen *M. paratuberculosis* would thus be unable to sustain itself in the herd. In other words, prevention is more cost-effective than “treatment”. In areas of the U.S. where dairy herds tend to be large, e.g., Western U.S., dairy producers typically do not use tests for paratuberculosis and instead rely on herd management to control the disease (USDA, 2005). Therefore, the model results reflect economic decisions regarding paratuberculosis control that U.S. dairy producers are making today.

Testing is an important component of paratuberculosis control strategies for the base herd and for most herds that may not be as labor efficient as the larger dairies. At higher herd hygiene levels the optimal producer decisions on test results generally include the manage branch as opposed to culling of test-positive cows. In contrast, for herds operating at lower herd hygiene levels the optimal decision on test results tends to include more culling. Some diagnostic tests, like C, D, and E suggest more culling as the optimal producer decision. However these tests are rarely the test of choice and will likely require subsidization if they are to become economical for dairy producers to incorporate into a paratuberculosis control program.

As with other paratuberculosis computer models, JD-Tree indicates that the test-and-cull strategy is not an economically attractive control method when applied

indiscriminately across all herds of diverse size, infection prevalence, herd hygiene level, or all diagnostic test types and level of test results. Instead, the model predicts that the most favorable strategy for paratuberculosis control is a program tailored to the specific farm that involves a specific combination of culling and managing test-positive cows depending on the herd prevalence and herd hygiene level.

The JD-Tree model appears to be an effective and flexible method for determining the most economical paratuberculosis control strategy for commercial dairy herds. Although the model remains to be validated in the field, it is currently a useful instructional tool helping veterinarians to understand the complex interactions affecting the economics of paratuberculosis control. This model could be strengthened by inclusion of probability distributions and at risk, provided valid field data were available to define those functions. The optimal paratuberculosis control program defined by JD-Tree almost always involves improvements in herd hygiene which may or may not be supported by diagnostic testing. In the absence of government subsidies for paratuberculosis testing, low cost diagnostics are favored by this economic model. Underlying model outcomes are critical assumptions about modes and frequency of *M. paratuberculosis* transmission. These assumptions are based on expert opinion and admittedly have limited field data to support them. Strengthening the biological assumptions in the model requires data from longitudinal field studies to better characterize *M. paratuberculosis* transmission in dairy herds.

Paratuberculosis experts and diagnosticians have experience in use of laboratory tests. Academic clinicians have experience and opinions about the best on-farm management practices. Veterinary practitioners have yet other views about farm management practices that clients will actually adopt. And, dairy producers who make economic decisions about their business on a daily basis have still other views about whether paratuberculosis control seems profitable. A convergence of these different perspectives on the outcomes and utility of the JD-Tree model will be the best demonstration of its validity.

## 5. Conclusion

JD-Tree is a useful instructional tool, helping veterinarians understand the complex interactions affecting the economics of paratuberculosis control and to define the accuracy and cost specifications of better diagnostic tests.

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